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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/549,590	09/20/2005	Takao Sato	930055-2035	1130

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Ronald R Santucci
Frommer Lawrence & Haug
745 Fifth Avenue
New York, NY 10151

EXAMINER	
HELM, CARALYNNE E	

ART UNIT	PAPER NUMBER
1615	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/549,590	SATO ET AL.	
	Examiner	Art Unit	
	CARALYNNE HELM	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 April 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-7,11,12,14-16 and 18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3-7, 11-12, 14-16, and 18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Withdrawal of Finality

The finality of the previously mailed Office action is hereby withdrawn in view of the new ground of rejection set forth below.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

The four factual inquires of Graham v. John Deere Co. have been fully considered and analyzed in the rejections that follow.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3, 5, and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Uno et al. (previously cited) in view of Aiache et al. (previously cited), Nishihara et al. (US PGPub No. 2002/0164379), Yasuda et al. (US Patent No.6,310,116), and Janda et al. (U.S. Patent No. 4,640,936 – previously cited).

Uno et al. teach a contact lens with a polymer consisting of a 2-hydroxyethyl methacrylate (HEMA - hydrophilic monomer having a hydroxyl group in its molecule), 2-hydroxy-3-methacryloyloxypropyl triammonium chloride (MAPTAC - monomers having a nitrogen atom in its side chain), mono-(2-acryloyloxyethyl) acid phosphate (MOAP), triethylene glycol dimethacrylate (monomer copolymerizable with the other monomers) (see paragraph 19 and table 1 example 6; instant claim 1). The MAPTAC is taught present at 5%, while the MOAP is present at 10 wt% (see table 1 example 6; instant claim 3). In addition, Uno et al. teach that mono-(2-acryloyloxyethyl) acid phosphate and 2-methacryloyloxyethyl acid phosphate (MOEP - Formula I/II) are functional equivalents (see paragraph 12; instant claim 1). Uno et al. do not explicitly teach that the resulting lens also contains a cationic group containing drug or the presence of a monomer of formula III along with the MOEP.

Aiache et al. teach the inclusion of several types of drugs in a polyHEMA hydrogel contact lens (see column 13 lines 29-35). Nishihara et al. teach a variety of drugs that are commonly used in ophthalmic compositions (see paragraph 121). In this set is included several cationic compounds including ephedrine hydrochloride, tetrahydrozoline hydrochloride, and naphazoline sulfate which also each include a secondary amine (see paragraph 122; instant claims 1 and 5).

Yasuda et al. teach molded articles composed of polymers made from hydrophilic monomers (see abstract). Both ophthalmic (contact) lenses and dental materials are contemplated as the end uses for these materials (see column 6 lines 31-34). Yasuda et al. go on to teach particular monomers that are contemplated for use individually or in combination that include HEMA, 2-methacryloyloxyethyl dihydrogen phosphate (MOEP-formula II) and bis(2-methacyloyloxyethyl) hydrogen phosphate (formula III) (see column 8 lines 17-19, 24-27, and 43-45). Janda et al. teach the use of both MOEP and bis-(methacryloyloxyethyl) hydrogen phosphate (formula III) in a polymeric preparation for biological use (dental adhesive) (see example and claim 1; instant claim 1). The proportion of the formula II in the formula II and formula III monomers is 50 wt% (see column 3 lines 1-15).

Since Uno et al. teach the equivalence of their phosphate containing monomers it would have been obvious to use MOEP in their exemplified composition instead of MOAP. In light of the teachings of Yasuda et al. and Janda et al. where the same combination of phosphate bearing, HEMA based hydrophilic monomers (where both MOEP and formula III are taught) can be used together in contact lenses or dental

materials, it also would have been obvious to use bis(2-methacyloyloxyethyl) hydrogen phosphate along with MOEP in the composition of Uno et al. as the phosphate bearing monomers. Since these monomers in Uno et al. serve the purpose of providing an anionic group containing monomer, it would have been obvious to use the pair at the proportion taught by Uno et al., namely 10 wt% (see paragraph 12; instant claim 16). The distinction between formula II and formula II is that formula III contains the repetition of the hydroxyethyl methacrylate moiety present in formula II only once. This difference in architecture would allow for the presence of phosphate groups within a contiguous polymer chain upon polymerization of formula III, as opposed to pendent from a polymer chain as polymerization of formula II yields. Although an equal proportion of these two monomers is taught by Janda et al., one of ordinary skill would have found it obvious to alter their relative ratio to control the final produce architecture and arrangement of charged groups in the final product (see instant claim 16). In addition, since the inclusion of an ophthalmic drug in contact lens was known in the art, it also would have been obvious to include a cationic drug in the resulting ophthalmic lens. Therefore claims 1, 3, 5, and 16 are obvious over Uno et al. in view of Aiache et al., Nishihara et al., Yasuda et al., and Janda et al.

Claims 1, 4, and 14-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Uno et al. in view of Aiache et al., Nishihara et al., Yasuda et al., and Janda et al. as applied to claims 1, 3, 5, and 16 above, and further in view of Ohmura et al. (previously cited)

Uno et al. in view of Aiache et al., Nishihara et al., Yasuda et al., and Janda et al. make obvious a contact lens with a cationic drug, and a copolymer made of HEMA, MAPTAC, MOEP, bis(2-methacyloyloxyethyl) hydrogen phosphate, and triethylene glycol dimethacrylate (see instant claims 1 and 15). Uno et al. teach the presence of a quaternary ammonium salt that is radically polymerizable in the polymer (see paragraph 12). In the example discussed, MAPTAC serves this function in the polymer. This modified reference does not teach that (meth)acrylamide is capable of performing the same function in the polymer.

Ohmura et al. teach a hydrophilic copolymer preparation where a set of vinyl monomers that are radically polymerizable is one of its monomers (see column 11 lines 51-54). In this set, MAPTAC, meth(acrylamide) and quaternary ammonium salts of methacrylic acid are taught to be functionally equivalent (see column 11 lines 63-64 and column 11 lines 67-column 12 line 37; instant claims 4 and 14). Since (meth)acrylamide can be used in the same role as the general class (quaternary ammonium salt that is radically polymerizable) and specific monomers taught by Uno et al., it would have been obvious to one of ordinary skill in the art to employ (meth)acrylamide instead of MAPTAC in the contact lens preparation of Uno et al. in view of Aiache et al., Nishihara et al. Yasuda et al., and Janda et al. Thus claims 1, 4, and 14-15 are obvious over Uno et al. in view of Aiache et al., Nishihara et al., Yasuda et al., Janda et al., and Ohmura et al.

Claims 1, 16, and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Uno et al. in view of Aiache et al., Nishihara et al., Yasuda et al., and Janda et al. as applied to claims 1, 3, 5, and 16 above, and further in view of Kamishita et al. (previously cited).

Uno et al. in view of Aiache et al., Nishihara et al., Yasuda et al., and Janda et al. make obvious a contact lens with a drug, and a copolymer made of HEMA, MAPTAC, MOEP, bis(2-methacyloyloxyethyl) hydrogen phosphate, and triethylene glycol dimethacrylate with the claimed proportions and ratios of monomers. Although the modified reference does teach other salt forms of naphazoline, it does not explicitly teach naphazoline nitrate specifically as the drug.

Kamishita et al. teach that naphazoline nitrate is a known drug that is used to treat ailments of the eye, (see column 3 lines 10-13; instant claim 18). Since this compound was known to be delivered to the eye and ophthalmic lens as the means of delivery were also known, it would have been obvious to one of ordinary skill in the art to employ naphazoline nitrate in an ophthalmic lens. In addition, since other salt forms were also known for delivery to the eye, one of ordinary skill in the art would have found it obvious to employ naphazoline nitrate as the cationic drug in Uno et al. in view of Aiache et al., Nishihara et al., Yasuda et al., and Janda et al. Thus claims 1, 16, and 18 are obvious over Uno et al. in view of Aiache et al., Nishihara et al., Yasuda et al., Janda et al., and Kamishita et al.

Claims 6 and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sulc et al. (previously cited) in view of Aiache et al. (previously cited).

Sulc et al. teach a contact lens (ophthalmic lens) as a drug delivery system where a cationic and anionic monomer pair is used (see column 5 lines 3-6; instant claim 6). Specifically Sulc et al. teach the lens made from a copolymer of N,N-dimethylaminoethyl methacrylate (anionic monomer), methacrylic acid (cationic monomer), HEMA (hydrophilic monomer), and ethylene glycol dimethacrylate (monomer copolymerizable with the other monomers) (see column 2 lines 66-67, column 3 lines 3-6 and 58-61, column 4 lines 22-25, and example 1; instant claim 6). Sulc et al. teach the anionic to cationic polymer ratio in one embodiment to be approximately 90 mol% (90.7 mol% as calculated by examiner from example 1). It would therefore have been obvious to one of ordinary skill in the art at the time of the invention to use the contact lens formulation of Sulc et al. with an anion-cationic monomer ratio of 90mol%. Sulc et al. do not teach particular drugs to use in the embodiment where the lens is also a drug delivery device.

Aiache et al. teach the inclusion of a sodium diclofenac, an anionic and carbonyl group containing drug, in a polyHEMA hydrogel contact lens (see example 7; instant claims 6 and 7). Thus in view of the teachings of Aiache et al. it would have been obvious to one of ordinary skill in the art at the time of the invention to employ sodium diclofenac in the invention of Sulc et al. Thus claims 6 and 7 are obvious over Sulc et al. in view of Aiache et al.

Claims 6, 11, and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sulc et al. in view of Aiache et al. as applied to claims 6 and 7 above and in further view of Lee et al. (Materials Science and Engineering C 2002 20:161-166), Atkinson et al. (EP 0032443), and Kato et al. (previously cited).

Sulc et al. in view of Aiache et al. make obvious an anionic drug containing contact lens with a copolymer consisting of a hydrophilic monomer, cationic monomers, anionic monomers and a monomer copolymerizable with these components such that the molar ratio of anionic monomer to cationic monomer is 30 to 90 mol%. Sulc et al. in view of Aiache et al. do not teach a water soluble azulene as one such anionic drug delivered from their device or explicitly teach a molar ratio of 40 mol% to 80 mol%.

Lee et al. teach that an anionic molecule contained within a cationic hydrogel is released slowly due to the electrostatic interaction between the opposite charges (see figure 3). Atkinson teaches that the presence of both cationic and anionic monomers in a hydrogel adds to its mechanical integrity via their ionic interaction (see page 7 lines 6-13 and tables 1 and 2). Thus the manipulation of the proportion of anionic to cationic monomer in the invention Sulc et al. would have been obvious to one of ordinary skill in the art to facilitate multiple results. The first result would be to allow for added mechanical integrity of the lens. Secondly, the amount of excess cationic charge controls the amount of anionic drug that can be retained long term (e.g. based on duration of dosing regimen or use) and slowly released from the lens. Such a parameter (result effective variable) would be obvious to optimize during the course or routine experimentation and based upon the desired end use (see instant claim 11).

Kato et al. teach that sodium azulene sulfonate (water soluble azulene) is a known drug that is used to treat ailments of the eye, such as inflammation (see column 2 lines 7-14; instant claim 12). Although Kato et al. teach this compound being delivered via eye drops, it would have been obvious to one of ordinary skill in the art at the time of the invention to use another known means of delivery, such as in a contact lens as taught by Aiache et al. and Sulc et al. Therefore it would have been obvious to use sodium azulene sulfonate instead of the particular drugs taught by Aiache et al. in the device of Sulc et al. Thus claims 6, 11, and 12 are obvious over Sulc et al. in view of Aiache et al., Lee et al., Atkinson et al., and Kato et al.

Response to Arguments

Applicants' arguments, filed April 16, 2009, have been fully considered and are persuasive in part. Several references relied upon previously (Wichterle et al. and Anderson et al.) that have been persuasively argued against have been removed from the grounds of rejection and new references are applied in the rejections presented above. References argued but still utilized in the rejections are addressed below.

Regarding rejections under 35 USC 103(a):

Applicant argues that the teachings of Janda et al. concerning dental adhesive compositions would not have been relied upon by one of ordinary skill in the art for the modification of a contact lens. In light of the teachings of Yasuda et al. that the same

hydrophilic monomers can be used in both contact lenses and dental materials, one would turn to Janda et al., who teach a collection of these monomers, for guidance as to proportions and particular combinations of monomers. In addition, applicant also argues that there would have been no motivation to alter the proportion of formula II relative to formula III in the composition. The distinction between formula II and formula II is that formula III contains the repetition of the HEMA moiety that is present in formula II only once. This difference in architecture would allow for the presence of phosphate groups within a contiguous polymer chain upon polymerization of formula III, as opposed to pendent from a polymer chain as polymerization of formula II yields. Since this different result would have been evident to one of ordinary skill in the art, the relative proportion of these monomers is a result effective variable and therefore subject to optimization via routine experimentation by one of ordinary skill in the art. Thus the claimed proportion of formula II relative to formula III would have been obvious from the teachings of Uno et al., Yasuda et al., and Janda et al.

Applicant's arguments regarding the error in classification of monomers by Sulc et al. are noted. However, in spite of example 17 not demonstrating the claimed proportion of anion (negatively charged) to cationic (positively charged) monomers, example 1 does. Example 1, lens A teaches N,N-dimethylaminoethylmethacrylate (DMAEMA) at 5.678 wt %, methacrylic acid (MAA) at 2.822 wt%, HEMA, and ethylene glycol dimethacrylate. Here DMEAMA is the cationic monomer, MAA is the anionic monomer, HEMA is the hydrophilic monomer and ethylene glycol dimethacrylate is the monomer polymerizable with these components. Since the molecular weight of

DMEAMA is 157 g/mol and that of MMA is 86 g/ml, these weight percentages correspond to a molar ratio of anionic to cationic monomer of 90.7%. Since this value is approximately 90%, one of ordinary skill in the art would have found it obvious to utilize a molar ratio for anionic to cationic monomers of 90%. Applicant argues that there is no motivation to optimize the ratio of charged monomers; however this argument is not persuasive. As indicated by the teachings of Lee et al. and Atkinson et al. the presence of charge in a drug releasing hydrogel, as is produces by Sulc et al., serves two known purposes, sequestering of oppositely charged drug and increased mechanical integrity of the hydrogel due to their ionic interaction. It would have been clear that the amount of excess charge (e.g. the molar ratio of cationic and anionic monomers) determines the amount of drug that can be held and the duration over which the drug is released. Therefore as a result effective variable, one of ordinary skill in the art would have had good reason to modify the molar ratio of anionic to cationic monomers in the invention of Sulc et al. to achieve a desired amount of drug loading and controlled release. Thus modification of the proportions taught by Sulc et al. would have been obvious to one of ordinary skill in the art. Applicant also argues that the teachings of Kato et al. would not have been relied upon to supply a particular drug because they are taught as non-essential components. As discussed in the previous response to arguments, the use of contact lenses as drug delivery devices was well known in the art at the time of the invention (see Chiou - US Patent No. 5,182,258 - column 3 lines 5-10, Schultz et al. - US Patent No. 6,410,045 - column 2 line 66-column 3 line 10, column 3 line 67-column 4 line 4, and column 5 lines 44-52). Kato et al. teach particular drugs and salt forms that

were known to be delivered to the eye. Thus it would have been obvious to one of ordinary skill to look to this reference for guidance regarding particular drugs that would be desirous to deliver to the eye from the contact lens of Sulc et al.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CARALYNNE HELM whose telephone number is (571)270-3506. The examiner can normally be reached on Monday through Thursday 8-5 (EDT).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on 571-272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Caralynne Helm/
Examiner, Art Unit 1615

/MP WOODWARD/
Supervisory Patent Examiner, Art Unit 1615